Compilation Of Designated Testimony That Implicates General Causation

I. Min Li

Witness	Date	Begin	End	Testimony
Min Li	4/21/2021	322:2 322:17	322:8 323:13	322:2 Q. On the screen is Exhibit 206, 322:3 which is the June 28, 2006 European Medicines 322:4 Agency Guidelines on the Limits of Genotoxic 322:5 Impurities, which was valid from January 1, 322:6 2007 to January 31, 2018. 322:7 Do you see that? 322:8 A. Mm-hmm. ***** 322:17 Q. Section 4 of this document from 322:18 the European Medicines Agency is titled 322:19 "Toxicological Background," and it states, 322:20 "According to current regulatory practice it 322:21 is assumed that (in vivo) genotoxic compounds 322:22 have the potential to damage DNA at any level 322:23 of exposure and that such damage may 322:24 lead/contribute to tumour development. Thus 323:1 for genotoxic carcinogens it is prudent to 323:2 assume that there is no discernible threshold 323:3 and that any level of exposure carries a 323:4 risk." 323:5 Do you see that? 323:6 A. Yes. 323:7 Q. NDMA is a genotoxic compound as 323:8 discussed here, correct? 323:9 A. Yes. 323:10 Q. NDEA is a genotoxic compound as 323:11 discussed here, correct? 323:12 [omitted from designation] 323:13 A. Yes.

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Min Li	4/21/2021	329:18	331:5	329:18 Q. Looking at the center of the 329:19 page, the first full paragraph, this EMA 329:20 document states, "Some structural groups were 329:21 identified to be of such high potency that 329:22 intakes even below the threshold of 329:23 toxicological concern would be associated 329:24 with a high probability of a significant 330:1 carcinogenic risk," and then there's 330:2 citations to two articles, one from 1999 and 330:3 one from 2004. 330:4 Do you see that? 330:5 A. Yes. 330:6 Q. A significant carcinogenic risk 330:7 would be a significant risk of developing 330:8 cancer. That's what that phrase means, 330:9 correct? 330:10 [omitted from designation] 330:11 [omitted from designation] 330:12 A. It says a high probability. 330:13 And again, although I haven't gone through 330:14 these two papers, but based upon everything, 330:15 you know, that I know, these results most 330:16 likely derived from animal studies. 330:17 [omitted from designation] 330:18 [omitted from designation] 330:19 When this refers to a 330:20 significant carcinogenic risk, that means by 330:21 definition a significant risk of developing 330:22 cancer, correct? That's what those words 330:23 mean, right? 330:24 [omitted from designation] 331:1 [omitted from designation] 331:2 A. It says, "a high probability of 331:3 a significant carcinogenic risk." It's still

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				331:4 a probability, although it's a high 331:5 probability.
Min Li	4/21/2021	333:10	333:22	333:10 Q. It was not acceptable to sell 333:11 valsartan with NDMA contamination because of 333:12 the high probability of a significant 333:13 carcinogenic risk, correct? 333:14 [omitted from designation] 333:15 [omitted from designation] 333:16 [omitted from designation] 333:17 A. You know, as I told you, you 333:18 know, once, you know, once we knew, you know, 333:19 in June 2018 and once we determined, you 333:20 know, the levels, we immediately, you know, 333:21 contacted regulatory agencies and take 333:22 actions.
Min Li	4/21/2021	381:13	382:17	381:13 Q. The title of this document is 381:14 "Assessment and Control of DNA Reactive 381:15 (Mutagenic) Impurities in Pharmaceuticals to 381:16 Limit Potential Carcinogenic Risk." And it 381:17 says then "M7." 381:18 Do you see that? 381:19 A. Mm-hmm. 381:20 Q. Just to be clear on the title 381:21 and the purpose of this document is to 381:22 prevent human beings from developing cancers 381:23 as a result of pharmaceutical drugs, correct? 381:24 [omitted from designation] 382:1 [omitted from designation] 382:2 A. It's already, you know, stated 382:3 very clear, right? It's for the purpose to 382:4 limit the potential carcinogenic risk. 382:5 [omitted from designation]

Witness	Date	Begin	End	Testimony
				382:6 Q. It's to limit the potential 382:7 carcinogenic risk for human beings ingesting 382:8 pharmaceutical products, correct? 382:9 A. Yes. 382:10 Q. More specifically, it's seeking 382:11 to limit that potential carcinogenic risk as 382:12 a result of DNA reactive or mutagenic 382:13 impurities in those pharmaceutical products, 382:14 correct? 382:15 [omitted from designation] 382:16 [omitted from designation] 382:17 A. Based upon this title, yes.
Min Li	4/21/2021	469:5	469:18	469:5 Q. This standard is talking about 469:6 impurities in pharmaceuticals. Those would 469:7 be pharmaceuticals that would be taken by 469:8 human beings, correct? 469:9 A. Yes. 469:10 Q. And with regard to humans 469:11 taking pharmaceuticals, this is talking about 469:12 certain impurities that display extremely 469:13 high carcinogenic potency. That's the 469:14 context, correct? 469:15 [omitted from designation] 469:16 [omitted from designation] 469:17 A. With regard to that, you know, 469:18 specific, you know, the three classes, yes.
Min Li	4/21/2021	471:13	472:14	471:13 Q. The FDA established limits of 471:14 96 nanograms, which equates to 0.3 parts per 471:15 million, correct? 471:16 A. Yes, for valsartan. 471:17 Q. For NDMA in valsartan, correct? 471:18 A. Versus its maximum dose, yes.

Witness	Date	Begin	End	Testimony
				471:19 Q. And for NDEA, actually 471:20 established limits of 26.5 nanograms or 471:21 .083 parts per million, correct? 471:22 [omitted from designation] 471:23 [omitted from designation] 471:24 A. Yeah, it looks like, yes. 472:1 [omitted from designation] 472:2 [omitted from designation] 472:3 [omitted from designation] 472:4 Q. These limits were set in order 472:5 to protect patient safety, correct? 472:6 [omitted from designation] 472:7 [omitted from designation] 472:8 [omitted from designation] 472:9 [omitted from designation] 472:10 [omitted from designation] 472:11 [omitted from designation] 472:12 A. As the title of this M7 472:13 implies, you know, the purpose is limit of 472:14 potential carcinogenic risk.
Min Li	4/22/2021	667:21	668:17	667:21 Q. I want to go through the 667:22 document a little bit, this article. First 667:23 we'll start in Section 12 titled "Previous 667:24 Evaluations By International Bodies." 668:1 And this states, "NDMA has been 668:2 classified by the International Agency for 668:3 Research on Cancer (IARC, 1987) as a 668:4 'probable human carcinogen (Group 2A),' based 668:5 upon sufficient evidence of a carcinogenic 668:6 effect in experimental animal species and the 668:7 demonstrated similarities in its metabolism 668:8 by human and rodent tissues." 668:9 Do you see that?

Witness	Date	Begin	End	Testimony
				668:10 A. Yes. 668:11 Q. And in terms of the risks to 668:12 humans as compared to animals, you certainly 668:13 don't disagree that there are similarities in 668:14 the metabolism of humans and rodents as 668:15 stated here, you certainly don't disagree 668:16 with that, right? 668:17 A. Whatever that statement says.
Min Li	4/22/2021	669:11	669:21	669:11 NDMA is a genotoxic substance, 669:12 correct? 669:13 [omitted from designation] 669:14 [omitted from designation] 669:15 A. It is. 669:16 [omitted from designation] 669:17 Q. NDEA is also a genotoxic 669:18 substance, correct? 669:19 [omitted from designation] 669:20 [omitted from designation] 669:21 A. Yes.
Min Li	4/22/2021	685:11	687:4	685:11 Q. You've mentioned animal studies 685:12 many times, and I think you made that point 685:13 multiple times. So why haven't there been 685:14 human studies done where humans have been 685:15 given NDMA to see what happens to humans? 685:16 A. That would be unethical. 685:17 Q. It would be unethical, right? 685:18 That's what you said? 685:19 A. Yes. 685:20 Q. Because -- 685:21 A. Knowingly, yes, if you 685:22 knowingly do that, yes. 685:23 [omitted from designation]

Witness	Date	Begin	End	Testimony
				685:24 [omitted from designation] 686:1 [omitted from designation] 686:2 Q. It would be unethical because 686:3 you would be increasing the risk that these 686:4 people would get cancer from having the NDMA 686:5 put into their body, right? 686:6 [omitted from designation] 686:7 [omitted from designation] 686:8 [omitted from designation] 686:9 A. As I think I already answered 686:10 that question. It's just considering the 686:11 potential risk. If you knowingly to do that 686:12 experiment, it will be unethical. 686:13 [omitted from designation] 686:14 Q. It would be unethical to 686:15 knowingly give humans NDMA, correct? 686:16 [omitted from designation] 686:17 [omitted from designation] 686:18 A. I think I already made that 686:19 clear. 686:20 [omitted from designation] 686:21 Q. And it would certainly be 686:22 unethical to give humans NDMA in the levels 686:23 that were found in the valsartan pills 686:24 deliberately and knowingly, correct? 687:1 [omitted from designation] 687:2 [omitted from designation] 687:3 [omitted from designation] 687:4 A. It's the same principle.
Min Li	4/22/2021	696:3	697:4	696:3 Q. Looking again at this article 696:4 cited by ZHP and relied on by ZHP in its 696:5 deviation investigation report, the top right 696:6 column on page 23 -- do you see where I am?

Witness	Date	Begin	End	Testimony
				696:7 A. The top right, the first 696:8 paragraph? 696:9 Q. Yes. 696:10 A. Okay, yeah, I see that. 696:11 Q. It says, "Therefore, owing to 696:12 the considerable evidence of carcinogenicity 696:13 of NDMA in laboratory species, evidence of 696:14 direct interaction with DNA consistent with 696:15 tumour formation, and the apparent lack of 696:16 qualitative species-specific differences in 696:17 the metabolism of this substance, NDMA is 696:18 highly likely to be carcinogenic to humans." 696:19 That's what this article 696:20 states, correct? 696:21 A. Yeah. Based upon, you know, 696:22 the last sentence, you know, you know, 696:23 another way to say is NDMA, you know, is a 696:24 probable, you know, carcinogen to human. 697:1 It's still the same thing. 697:2 Q. Yeah. Probable, yeah. 697:3 A. Highly likely, you know, is 697:4 probable.
Min Li	4/22/2021	699:24	700:11	699:24 Q. At the levels of contamination 700:1 that we've gone through in this deposition, 700:2 it would be unacceptable and, using your 700:3 word, unethical to sell valsartan with those 700:4 levels of NDMA contamination, correct? 700:5 [omitted from designation] 700:6 [omitted from designation] 700:7 [omitted from designation] 700:8 [omitted from designation] 700:9 [omitted from designation] 700:10 A. You know, as I said, you know,

Witness	Date	Begin	End	Testimony
				700:11 if you knowingly do that, okay.

II. Jucai Ge

Witness	Date	Begin	End	Testimony
Jucai Ge	5/27/2022	174:18	175:2	174:18 Q. Looking again at the Gomm[1] 174:19 study, which you yourself brought to this 174:20 deposition, in the middle of the right-hand 174:21 side under the heading Regulatory and public 174:22 health implications, the second-to-last 174:23 sentence says, "The immediate recall of all 174:24 potentially NDMA-contaminated valsartan drug 175:1 products by regulatory authorities worldwide 175:2 was necessary [rest of sentence omitted from designation]

[1] This is a reference to Gomm W, Röthlein C, Schüssel K, Brückner G, Schröder H, Heß S, Frötschl R, Broich K, Haenisch B. N-Nitrosodimethylamine-Contaminated Valsartan and the Risk of Cancer—A Longitudinal Cohort Study Based on German Health Insurance Data. Dtsch Arztebl Int. 2021 May 28;118(21):357-362. doi: 10.3238/arztebl.m2021.0129. PMID: 34247699; PMCID: PMC8372009.

III. Peng Dong

Witness	Date	Begin	End	Testimony
Peng Dong	3/29/2021	45:8	46:11	45:8 Q. When Section 4.3.1 refers to 45:9 the "technical departments" plural, that 45:10 includes the technical department at 45:11 Chuannan, correct? 45:12 [omitted from designation] 45:13 A. After this SOP became 45:14 effective, all the technical departments 45:15 referred to under Section 4.1 point – 45:16 [omitted from designation] 45:17 [omitted from designation] 45:18 A. -- under Section 4.3.1, 45:19 including the technical department in 45:20 Chuannan, need to conduct their work based on 45:21 the effective SOP at that time. 45:22 [omitted from designation] 45:23 Q. Look at 4.4.1. The first part 45:24 says, "Genotoxic substances are potentially 46:1 destructive to DNA at any intake level, and 46:2 this damage may lead to tumors." Correct? 46:3 It says that in part, correct? 46:4 [omitted from designation] 46:5 A. One sentence under 46:6 Section 4.4.1 of this document does say that 46:7 "Genotoxic substances are potentially 46:8 destructive to DNA at any intake level, and 46:9 this damage may lead to tumors." 46:10 This sentence is only within 46:11 this paragraph under Section 4.4.1.

Witness	Date	Begin	End	Testimony
Peng Dong	4/1/2021	370:24	371:19	370:24 Q. On the screen is Exhibit 206, 371:1 which is the guideline that we just discussed 371:2 from the EMEA, and I'd like to turn now to 371:3 Section 4 on page 4 of 8 at the very top. 371:4 The first paragraph under 371:5 Section 4, which is titled "Toxicological 371:6 Background," says, "According to current 371:7 regulatory practice it is assumed that 371:8 (in vivo) genotoxic compounds have the 371:9 potential to damage DNA at any level of 371:10 exposure and that such damage may 371:11 lead/contribute to tumor development. Thus 371:12 for genotoxic carcinogens it is prudent to 371:13 assume that there is no discernible threshold 371:14 and that any level of exposure carries a 371:15 risk. " 371:16 My question is, since your 371:17 company consulted this standard in 2011, your 371:18 company knew the information I just read, 371:19 correct?
Peng Dong	4/1/2021	382:14	382:20	382:14 Q. At the very bottom of page 2, 382:15 this refers to "a class of very potent 382:16 genotoxic carcinogens," and that includes, 382:17 according to this, N-nitroso compounds. 382:18 You agree that a N-nitroso 382:19 compound is a very potent genotoxic 382:20 carcinogen, correct?

IV. Xiaodi Guo

Witness	Date	Begin	End	Testimony
Xiaodi Guo	5/20/2021	176:3	176:9	176:3 Q. Do you see in this article that 176:4 you are listed as an author of, I've highlighted the 176:5 sentence, it says: "Compared with other impurities in 176:6 drugs, genotoxic impurities pose serious hazards to 176:7 drug users even in trace amounts." 176:8 Do you see that? 176:9 A. Yes, yes.

V. Eric Gu

Witness	Date	Begin	End	Testimony
Eric Gu	4/6/2021	366:8	366:16	366:8 Q. As of the date of this 366:9 letter, November 2018, ZHP had determined 366:10 that dimethylamine was required for the 366:11 probable human carcinogen NDMA to form 366:12 during the valsartan API manufacturing 366:13 process, correct? 366:14 A. You say that very correct. 366:15 It's a probable human carcinogen. 366:16 Probable.
Eric Gu	4/6/2021	386:12	386:21	386:12 Q. ZHP would have been aware 386:13 these guidelines were put out in 2007 and 386:14 ZHP would have known as of 2007 that 386:15 nitrosamines, including NDEA and NDMA 386:16 belonged to a class of very potent 386:17 genotoxic carcinogens as of that time in 386:18 2007, correct? 386:19 [omitted from designation] 386:20 [omitted from designation] 386:21 THE WITNESS: You said it.

VI. Lijie Wang

Witness	Date	Begin	End	Testimony
Lijie Wang	1/26/2021	78:1	78:4	78:1 Q. Tell me your understanding 78:2 of what genotoxicity means. 78:3 A. Genotoxicity means that is 78:4 toxic material and may cause cancer.
Lijie Wang	1/26/2021	80:3	80:16	80:3 Q. Do you agree with me that 80:4 Prinston is not allowed to sell and never 80:5 has been allowed to sell drugs in the 80:6 United States that have genotoxic 80:7 impurities that pose a risk to human 80:8 health? 80:9 [omitted from designation] 80:10 [omitted from designation] 80:11 THE WITNESS: We want to 80:12 ensure -- we always want to ensure 80:13 our product meet the guidance on 80:14 the risk assessment based on FDA 80:15 guidance, including the topic 80:16 impurities.
Lijie Wang	1/26/2021	82:15 83:17	83:4 83:20	82:15 Q. At all 82:16 times, has Prinston relied on ZHP, the 82:17 manufacturer of the API, to assess 82:18 whether there were any unsafe genotoxic 82:19 impurities to the valsartan? 82:20 [omitted from designation] 82:21 [omitted from designation] 82:22 THE WITNESS: We rely on the 82:23 manufacturer. 82:24 [omitted from designation] 83:1 Q. And at no time did Prinston 83:2 do an independent assessment of the

Witness	Date	Begin	End	Testimony
				83:3 valsartan to determine whether there were 83:4 unsafe genotoxic impurities, correct? ***** 83:17 THE WITNESS: Prinston is 83:18 the ANDA holder. We rely on the 83:19 manufacturer to assess their 83:20 products.
Lijie Wang	1/26/2021	152:19	153:9	152:19 Q. NDMA and NDEA are n-nitroso 152:20 compounds, correct? 152:21 [omitted from designation] 152:22 [omitted from designation] 152:23 THE WITNESS: Yes, I believe 152:24 so, if I see the formulation of 153:1 the compounds. 153:2 BY MR. SLATER: 153:3 Q. So since NDMA and NDEA are 153:4 n-nitroso compounds, they are included in 153:5 the group identified here as 153:6 quote-unquote high potency mutagenic 153:7 carcinogens that comprise the cohort of 153:8 concern, according to this document, 153:9 correct?